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EXAMINER	
NIEBAUER, RONALD T	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,532	RAPP ET AL.	
	Examiner	Art Unit	
	Ronald T. Niebauer	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34 and 36-46* is/are pending in the application.

4a) Of the above claim(s) *26-34 and 38-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/7/05, 10/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1 (claims 1-25,36-37) and the following species: solid support – polystyrene; spacer – polyethylene glycol; ligand - the second formula set forth in claim 13 wherein the binding unit is Lys(Arg)2 in the reply filed on 12/13/07 is acknowledged.

The elected species, as currently interpreted (see 112 2nd below) was not found in the prior art. It is noted that Kasai et al. (Bioorganic and Medicinal Chemistry Letters 12 (2002) 951-954 as cited in IDS) teach branched lysine residues and arginine surface groups (Figure 1, page 953 first full paragraph) used during solid phase syntheses (i.e. with a support and spacer, but not the elected spacer) which includes (but does not consist of) the elected species of ligand. It is noted that no claims are drawn solely to the elected species.

The procedure for examination of Markush type claims is highlighted in MPEP section 803.02:

> Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable, the provisional election will be given effect and examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.
>
> On the other hand, should the examiner determine that the elected species is allowable, the examination of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species.
>
> The examination will be extended to the extent necessary to determine patentability

> of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action can be made final unless the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p).

In accord with section 803.02 of the MPEP, the examination was extended to other species and prior art was found (see below).

Claims 26-34,38-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/13/07.

Claim 35 has been cancelled.

Claims 1-25,36-37 are under consideration.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Sweden on 7/8/02. It is noted, however, that applicant has not filed a certified copy of the 020114-5 application as required by 35 U.S.C. 119(b).

Specification

The disclosure is objected to because of the following informalities:

The use of trademarks (page 30 Table 1 for example) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Appropriate correction is required.

The abstract of the disclosure is objected to because the abstract recites 'space' (last sentence). To be consistent with the claims and specification it appears that applicant is referring to a 'spacer'. Correction is required. See MPEP § 608.01(b).

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: figure 8 and figure 10 are correctly labeled, however the figure in between figure 8 and 10 (presumably figure 9) has not been labeled. Therefore the reference to figure 9 on page 16 of the specification is unclear. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 20,21, and 25 are objected to because of the following informalities:

Claim 20 and dependent claim 21 recite 'has a swelling capacity enough to allow'. The grammar used in the claim seems inappropriate. A recititation of 'has enough swelling capacity to allow' seems appropriate.

Claim 25 recites 'the at least one each binding unit is arginine'. The grammar used in the claim seems inappropriate. A recititation of 'the at least one binding unit is arginine' seems appropriate.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3,13,15-17,23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3,16, and 17 each recite various components of the matrix and 'derivatives thereof'. Derivatives thereof (section 0096) has been defined such that the meets and bounds of the term is unclear. One of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 3 recites the general formulas I and II. Both general formula I and II include the use of a semicolon inside of the brackets. The meaning of the semicolon is unclear. When

representing chemical structures a dash is typically used (as in the instant case) to represent a bond between elements, however the use of a semicolon is not commonly used. The applicant has not clearly set forth the formulas of claim 3. Further, formula II includes 2 left brackets (i.e. [[) however, only one right bracket (i.e.]) is used. As such it is unclear which subscripts correspond to which variables. Further, the applicant uses the subscript ½(m+1). When k is 0 then m is 0 and the subscript is equal to ½. It is unclear what a subscript of ½ means. Typically a subscript refers to the number of occurrences of a particular functional group. As claimed it is unclear what a fraction of a functional group would mean.

Claim 13 recites, at numerous locations, values for k. However, it is not clear if the k is meant to be part of a particular formula or if the k refers to something else. Applicant uses the abbreviations alpha and epsilon and states that (section 0095) the variables refer to nomenclature commonly used for amino acids. However, the attachment location of the spacer is unclear. For example, the applicant elected a species with a spacer of PEG and a binding unit of Lys(Arg)2. However, it is unclear is the PEG spacer is attached to the alpha carbon of the Lys or if the PEG is attached to the carboxy group of the lysine.

Claim 15 and dependents 16-17 recite the phrase 'is substantially hydrophobic or hydrophilic'. However, the metes and bounds of the term 'substantially' have not been set forth in the claim or the specification and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 23 recites 'wherein said polymer matrix has a cut-off value ranging...'. As claimed it is unclear if the value is referring to the molecular weight of the components of the matrix or if the value is referring to some type of property of the matrix. The metes and bounds of the term

'substantially' have not been set forth in the claim or the specification and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-4,12,14-24,36-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.
>
> Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of

such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a matrix comprising a ligand, a spacer, and a support (claim 1).

(1) Level of skill and knowledge in the art:

The level of skill in the art is high.

(2) Partial structure:

The ligand is described in claim 3 as having a certain formula. Although the formula is unclear (see 112 2nd), the genus is clearly broad since Y can be amino acids, peptides, fatty acids, carbohydrates, lectin, nucleotides, derivatives thereof (broadly defined in section 0096) and combinations thereof. Hence, there is substantial variability in the genus. Specific examples are provided in, for example, claim 13 in which the amino acids Arg, Lys, and Cys are part of the ligand. However, the examples are not representative of the genus. The examples only represent a small subset of amino acids. The examples do not represent any derivatives of amino acids or combinations with nucleotides, for example. There are no examples of nucleotide ligands or derivatives of nucleotide ligands ,for example. In addition to lack of description of the ligand, there are many possibilities for the spacer including derivatives thereof (see claim 15-17 for example). Although examples of spacers are provided in claims 16-17, for example PEG, adequate examples of derivatives thereof have not been provided.

Taken together, there is substantial variability in the genus. Since there are a substantial variety of ligands and spacers possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The ligand is described as having a binding unit (claim 1) and being complementary to other structures (claim 2, 22), for example. The ligand is described as including a derivative thereof (claim 3) (broadly defined in section 0096). What constitutes a derivative has not been clearly set forth. Taken together, the properties described do not adequately describe the ligand itself. From the description provided, there is no common core for all the possible ligands. Further there has been no correlation provided between the structure and the functional properties.

(5) Method of making the claimed invention:

Examples one and two, for example, describe making the invention, however the examples are not representative number of the full genus including ligands, derivitives thereof or combinations thereof.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) **1-**4,12,14-24,36-37 is/are broad and generic, with respect to all possible ligands and derivatives thereof encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because

there is no disclosure of a correlation between function and structure of the ligands beyond those ligands specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of ligands identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of ligands embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736; F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7,10,12-15,20-24,36 are rejected under 35 U.S.C. 102(a) as being anticipated by Kasai (Bioorganic and Medicinal Chemistry Letters 12 (2002) 951-954 as cited in IDS; document published on March 25,2002).

Kasai teach the synthesis of dendritic macromolecules using lysine as the branching unit and arginine as the surface group (page 953 first full paragraph, figure 1). Kasai teach (note 20 on page 954 and page 953 first full paragraph) the use of a Wang resin, the coupling of Gly, and the further coupling of Lys and Arg. As such, the Wang resin meets the limitations of a solid support, the glycine acts as a spacer, and the ligand is the Lys/Arg dendrimer (compare claim 1,36 of the instant invention). The ligand (comprises arginine) meets the limitations of claims 2, 3 (upon initial synthesis formula 1 where n is 0, k is 0, X1,X2,X3 being optional are not present, Z is the amino acid arginine), 4, 5, 6, 7, 12 (carboxy group) of the instant invention. Further, since Kasai teach dendrimers with, for example, 15 amino acids in addition to the spacer (TX-1943 of figure 1) the limitations of claims 10,14 are met, further the intermediate products (see note 20 of page 954) also read on claim 10. The dendrimer TX-1944 of Figure 1 includes Lys(Arg)2 as in the second structure of claim 13 of the instant invention. It is noted that 'has a tree- or comb-like structure' has been interpreted as open language (compare other transitional phrases such as 'having' in section 2111.03 of the MPEP).

Although unclear (see 122 2nd above) claims 3,13,15 and 23 have been given the broadest reasonable interpretation. The glycine spacer is regarded as substantially hydrophobic (compare claim 15 of the instant invention). Further, it is noted that the matrix of Kasai meets the structural limitations so the matrix must necessarily meet the functional limitations (for example, claims 20-24 of the instant invention) (see MPEP 2112.01).

Claims 1-9,11-13,15-24,36-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Nur et al. (US 2003/0124703).

Nur teach methods for removing plasmin or plasmin(ogen) that use an amino acid bound to a support (claim 1). Nur teach that the support can be polystyrene (claim 5) and the amino acid can be attached via a linker (claim 8). Nur specifically teach a sepharose – CNBr – arginine matrix (section 0055-0059) and a sepharose – epoxy – arginine matrix (section 0063-0066). Nur teach the CNBr/epoxy as the spacer (Table 2), therefore the sepharose is the solid support, CNBr/epoxy is the spacer and arginine is the ligand (compare claim 1, 13 (the first structure shown) of the instant invention). Nur teach the concentration of arginine at 0.01 mmol/ml dry gel (compare claims 8-9,11 of the instant invention). Further, the ligand (arginine) meets the limitations of claims 2, 3 (formula 1 where n is 0, k is 0, X1,X2,X3 being optional are not present, Z is the amino acid arginine), 4, 5, 6, 7, 12 (carboxy group) of the instant invention. The spacers described by Nur (epoxy/CNBr) (Table 2) meet the limitations of claims 15, 16 (epoxy can be regarded as a derivative of PEG), 17 (epoxy can be regarded as a derivative of PEG). The solid support described by Nur in claim 5 meets the limitations of claim 18. Nur teach the support in the form of a gel (section 0056) (compare claim 19 of the instant invention) which is capable of swelling (50ml of buffer and 2.5 g gel) (section 0057) (compare claim 20-21 of the instant invention). Nur teach the matrix in a tube (section 0058) and teach the matrix in a syringe cylinder which is regarded as a device (compare claims 36-37 of the instant invention). Further, it is noted that the matrix of Nur meets the structural limitations so the matrix must necessarily meet the functional limitations (for example, claims 22-24 of the instant invention) (see MPEP

2112.01). Although unclear (see 122 2nd above) claims 3,13,15 and 23 have been given the broadest reasonable interpretation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nur et al. (US 2003/0124703) as applied to claims 1-9,11-13,15-24,36-37 above, and further in view of Barany et al. (WO 92/04384 as cited in IDS).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

As discussed above Nur teach methods for removing plasmin or plasmin(ogen) that use an amino acid bound to a support (claim 1). Nur teach that the support can be polystyrene (claim

5) and the amino acid can be attached via a linker (claim 8). Nur specifically teach a sepharose – CNBr – arginine matrix (section 0055-0059) and a sepharose – epoxy – arginine matrix (section 0063-0066). Nur teach the CNBr/epoxy as the spacer (Table 2), therefore the sepharose is the solid support, CNBr/epoxy is the spacer and arginine is the ligand (compare claim 1, 13 (the first structure shown) of the instant invention). Nur teach the concentration of arginine at 0.01 mmol/ml dry gel (compare claims 8-9,11 of the instant invention). Further, the ligand (arginine) meets the limitations of claims 2, 3 (formula 1 where n is 0, k is 0, X1,X2,X3 being optional are not present, Z is the amino acid arginine), 4, 5, 6, 7, 12 (carboxy group) of the instant invention. The spacers described by Nur (epoxy/CNBr) (Table 2) meet the limitations of claims 15, 16 (epoxy can be regarded as a derivative of PEG), 17 (epoxy can be regarded as a derivative of PEG). The solid support described by Nur in claim 5 meets the limitations of claim 18. Nur teach the support in the form of a gel (section 0056) (compare claim 19 of the instant invention) which is capable of swelling (50ml of buffer and 2.5 g gel) (section 0057) (compare claim 20-21 of the instant invention). Nur teach the matrix in a tube (section 0058) and teach the matrix in a syringe cylinder which is regarded as a device (compare claims 36-37 of the instant invention). Further, it is noted that the matrix of Nur meets the structural limitations so the matrix must necessarily meet the functional limitations (for example, claims 22-24 of the instant invention) (see MPEP 2112.01). Although unclear (see 122 2nd above) claims 3,13,15 and 23 have been given the broadest reasonable interpretation.

Nur does not expressly teach PEG as a spacer as in claim 25 of the instant invention.

Barany teaches supports including polystyrene (the support) (figure 1a, claim 5), PEG (the linker) (Figure 1a) attached to a protein (the ligand) (page 14 last paragraph). Barany specifically teach the polystyrene-PEG (PEG-PS) support for synthesis of calcitonin (page 14 last paragraph). Barany teach PEG having an average molecular weight of 2000 daltons (last paragraph page 13). In example 10, PEG-PS resulted in better purity of the product (page 22) and Barany teach other desirable features of the PS-PEG supports (page 12 first full paragraph). Since Nur teach that an 'adequate spacer' (section 0006) can be used and teach a variety of linkers (section 0040) one would be motivated to substitute the specific linker as described by Barany because Barany teach numerous advantages of the particular linker. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

It has been recently held that "Neither §103's enactment nor *Graham*'s analysis disturbed the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art." KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The KSR court stated that "a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR at 1389.

Furthermore, The KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, Nur specifically teach a sepharose – CNBr – arginine matrix (section 0055-0059) while Barany teaches polystyrene-PEG-calcitonin (page 14 last paragraph). The claim would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, one would have substituted the polystyrene-PEG support of Barany for the sepharose-CNBr support of Nur to arrive at polystyrene-PEG-arginine (compare claim 25 of the instant invention). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ormum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7,12,14-24,36-37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,774,102 ('102) in view of Barany et al. (WO 92/04384 as cited in IDS).

'102 teach an adsorbent comprising a ligand immobilized on a solid support for endotoxin removal, the ligand consisting essentially of at least one oligopeptide (claim 1). '102 teach the support medium in the form of beads (claim 3) and teach arginine as an amino acid (claim 8). '102 teach a device comprising an adsorbent (claim 9).

'102 does not expressly teach a spacer as part of the adsorbent.

Barany teaches supports including polystyrene (the support) (figure 1a, claim 5), PEG (the linker) (Figure 1a) attached to a protein (the ligand) (page 14 last paragraph). Barany specifically teach the polystyrene-PEG support for synthesis of calcitonin (page 14 last paragraph). Barany teach PEG having an average molecular weight of 2000 daltons (last paragraph page 13). In example 10 PEG-PS resulted in better purity of the product (page 22) and teach other desirable features of the PS-PEG supports (page 12 first full paragraph). Since Barany numerous advantages of the particular linker one would be motivated to substitute the specific linker as described by Barany into the adsorbent of '102. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

It has been recently held that "Neither §103's enactment nor *Graham*'s analysis disturbed the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art." KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The KSR court stated that "a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR at 1389.

Furthermore, The KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, '102 specifically teach a support-oligopeptide (claim 1) while Barany teaches polystyrene-PEG-calcitonin (page 14 last paragraph). The claim would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, one would have substituted the polystyrene-PEG support of Barany for the support of '102 to arrive at polystyrene-PEG-oligopeptide (compare claim 1 of the instant invention). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

The ligand (comprising arginine, claim 8 of '102) meets the limitations of claims 2, 3 (during initial synthesis formula 1 where n is 0, k is 0, X1,X2,X3 being optional are not present, Z is the amino acid arginine), 4, 5, 6, 7, 12 (carboxy group) of the instant invention. The oligopeptides of '102 meet the limitations of claim 14. The PEG spacer of Barany (Figure 1a, last paragraph page 13) meets the limitations of claims 15-17. The polystyrene of Barany (Figure 1a) meets the limitations of claim 18. '102 teach the adsorbent in the form of beads (claim 3) meeting the limitations of claim 19.Further, it is noted that the polystyrene-PEG-oligopeptide meets the structural limitations so it must necessarily meet the functional limitations (for example, claims 20-24 of the instant invention) (see MPEP 2112.01). '102 teach a device comprising an adsorbent (claim 9) meeting the limitations of claim 36 of the instant invention.

Although unclear (see 122 2nd above) claims 3,13,15 and 23 have been given the broadest reasonable interpretation.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Schaeffer et al. (US 4,111,838) cited previously remains of record. Any rejection with Schaeffer would be duplicative of the rejections recited above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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